

**REMARKS**

Claims 1-22 are currently pending in the Application. Applicants have amended claims 1, 9, 12-16, 18 and 22 and added claims 45-47 to better claim the invention. No new matter has been added. Claims 23-44 have been canceled without prejudice. The Applicants reserve the right to reassert claims 23-44 in a continuation and/or a divisional application. Among the remaining claims, claims 1, 9, 16 and 45-46 are independent.

**I. Objection to the Specification**

In the Office Action, the Examiner had objected to embedded hyperlinks contained in the Specification (Office Action, page 3). Applicants have amended the Specification to remove the embedded hyperlinks at page 20, lines 13 and 14. No new matter has been added. Applicants respectfully request reconsideration and withdrawal of the above objection to the Specification.

**II. Provisional Double Patenting Rejection**

In the Office Action, the Examiner has provisionally rejected claims 1-22 under 35 U.S.C. §101 alleging that claims 1-22 claim the same invention as that of claims 1-19 of co-pending United States Patent Application Number 10/783,628 (Attorney Docket No. MWS-108). (Office Action, page 6). Since the rejection is provisional, Applicants will respond to the rejection when the rejection is made non-provisional.

In the Office Action, the Examiner has further provisionally rejected claims 1-22 under 35 U.S.C. §101 alleging that claims 1-22 claim the same invention as that of claims 1-19 of co-pending United States Patent Application Number 10/783,552 (Attorney Docket No. MWS-109). (Office Action, page 7). Since the rejection is provisional, Applicants will respond to the rejection when the rejection is made non-provisional.

**III. Claim Rejections under 35 U.S.C. §101**

In the Office Action, the Examiner has rejected claims 1-22 under 35 U.S.C. §101 claiming that the claims do not produce a tangible result (Office Action, pages 3-5). Applicants' claim 1 recites: "a storage component for storing the graphical model of the biological system."

Applicants' claim 9 recites: "storing the graphical model of the biological system." Applicants' claim 16 recites: "storage means for storing the graphical model of the biological system." Claims 2-8 depend from claim 1, claims 10-15 depend from claim 9 and claims 17-22 depend from claim 16 and as such incorporate all of the features of the claims from which they depend. Therefore for reasons set forth above, Applicants respectfully urge that claims 1-22 produce a useful, concrete and tangible result, and respectfully request reconsideration and withdrawal of the above 35 U.S.C. §101 rejection of claims 1-22.

#### **IV. Claim Rejections under 35 U.S.C. §102**

In the Office Action, the Examiner has rejected claims 1-22 under 35 U.S.C. §102(b) as being anticipated by United States Patent Publication Number 2002/0022947 (hereafter "Kurata"). Applicants respectfully traverse this rejection.

##### **A. Claim 1**

Applicants' claim 1 recites:

1. A system for improved simulation of a biological system comprising a plurality of chemical reactions, the system comprising:
  - a modeling component for *constructing a graphical model of a biological system including a first chemical reaction and a second chemical reaction, the graphical model including a specified constraint provided in addition to the chemical reactions that constrains dynamic behavior of the biological system*;
  - a storage component for storing the graphical model of the biological system; and
  - a simulation engine accepting as input said constructed graphical model of the biological system and generating as output dynamic behavior of the biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint.*

Applicants respectfully urge that Kurata does not disclose *constructing a graphical model of a biological system including a first chemical reaction and a second chemical reaction, the graphical model including a specified constraint provided in addition to the*

*chemical reactions that constrains dynamic behavior of the biological system and a simulation engine accepting as input said constructed graphical model of the biological system and generating as output dynamic behavior of the biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint*, which are present in Applicants' claim 1.

Applicants respectfully urge that Kurata does not disclose *constructing a graphical model of a biological system including a first chemical reaction and a second chemical reaction* because Kurata does not address graphical models of biological systems.

Kurata relates to simulating a biological system by dividing the biological system into two phases: the binding and reaction phases (Kurata, abstract). This method is called the two-phase partition method (Kurata, abstract). As illustrated in Figure 1 of Kurata, a chemical reaction formula that expresses a molecular network is input and partitioned into the binding and reaction phases (Kurata, paragraph [0040]).

In Figure 1, Kurata discusses receiving as input a chemical reaction formula that expresses a molecular network in the biological system. In subsequent steps, the reaction formula is partitioned and undergoes numerical formula conversion (Kurata, Figure 1). Kurata only discusses a mathematical model of a biological system. Kurata does not disclose a graphical model for representing the biological system. Therefore, Kurata does not disclose Applicants' claimed *constructing a graphical model of a biological system including a first chemical reaction and a second chemical reaction*.

In addition, Kurata does not disclose *the graphical model including a specified constraint provided in addition to the chemical reactions that constrains dynamic behavior of the biological system*, which is present in claim 1.

Kurata discloses receiving a chemical reaction formula that expresses a biological system. (Kurata, paragraph [0040]). Kurata also discloses that the chemical reaction formula is divided into two phases: the binding and reaction phases, and undergoes numerical formula conversion (Kurata, abstract).

In contrast, Applicants claim a graphical model that includes *a specified constraint provided in addition to the chemical reactions that constrains dynamic behavior of the biological system*. In an example embodiment, the constraint may be an algebraic equation that constrains the variables of the biological system. (Specification, pages 25-26). Kurata does not disclose *a constraint provided in addition to the chemical reactions that constrains dynamic behavior of the biological system*. In Kurata, the biological system is expressed by chemical reaction formulas. There is no disclosure in Kurata of a constraint that is provided in addition to the chemical reactions.

Regarding Applicants' claimed *a simulation engine accepting as input said constructed graphical model of the biological system and generating as output dynamic behavior of the biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint*, Applicants urge that Kurata does not disclose this feature of claim 1.

Kurata discloses a single chemical reaction formula expressed in Eq. (1) that is partitioned into the binding and reaction phases (Kurata, Figure 1). The two parts of the formulas undergo numerical formula conversion for equations that express the binding and reaction phases (Kurata, paragraph [0040]). The simulation is then executed based on the equations converted in the numerical formula conversion process (Kurata, paragraph [0040]).

Kurata, however, does not disclose *a first type of computational model for the first chemical reaction and a second type of computational model for the second chemical reaction*, which is present in claim 1. In Kurata, a single chemical reaction formula is divided into different equations (Kurata, Eq. (1) and Figure 1). Kurata, however, does not disclose different equations for different chemical reactions.

Furthermore, Kurata does not disclose *a simulation engine that uses a specified constraint to generate a dynamic behavior of the biological system*. As discussed above, Kurata does not disclose that the model includes a constraint (provided in addition to the chemical reactions) that constrains dynamic behavior of the biological system. Therefore, Kurata does not disclose "a simulation engine ... generating as output dynamic behavior of the biological system using ... the specified constraint," as is present in claim 1.

For at least the reasons set forth above, Applicants urge that Kurata does not anticipate Applicants' claim 1 under 35 U.S.C. §102(b). Therefore, Applicants respectfully request that the above 35 U.S.C. §102(b) rejection of claim 1 be withdrawn.

**B. Claims 2-8**

Claims 2-8 depend from independent claim 1 and, as such, incorporate all of the features of claim 1. Therefore, for at least the reasons set forth above with respect to claim 1, Applicants respectfully request that the above 35 U.S.C. §102(b) rejection of claims 2-8 be withdrawn.

**C. Claim 9**

Applicants' claim 9 recites:

9. An improved method for simulation of a biological system including a first chemical reaction and a second chemical reaction, the method comprising the steps of:
  - (a) *constructing a graphical model of the biological system including a first chemical reaction and a second chemical reaction, the graphical model including a specified constraint provided in addition to the chemical reactions that constrains dynamic behavior of the biological system;*
  - (b) storing the graphical model of the biological system; and
  - (c) *generating dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction and the specified constraint.*

Applicants respectfully urge that Kurata does not disclose *constructing a graphical model of the biological system including a first chemical reaction and a second chemical reaction*, which is present in claim 9. As discussed above with respect to claim 1, Kurata does not disclose *a graphical model of a biological system including a first chemical reaction and a second chemical reaction*. Also, as discussed above, Kurata does not disclose *the graphical model including a specified constraint provided in addition to the chemical reactions that constrains dynamic behavior of the biological system and generating dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction and the specified constraint*, which are present in claim 9.

For reasons set forth above, Applicants respectfully urge that Kurata does not anticipate Applicants' claim 9 under 35 U.S.C. §102(b). Therefore, Applicants respectfully request that the above 35 U.S.C. §102(b) rejection of claim 9 be withdrawn.

#### **D. Claims 10-15**

Claims 10-15 depend from independent claim 9 and, as such, incorporate all of the features of claim 9. Therefore, for at least the reasons set forth above with respect to claim 9, Applicants respectfully request that the above 35 U.S.C. §102(b) rejection of claims 10-15 be withdrawn.

#### **E. Claim 16**

Applicants' claim 16 recites:

16. An article of manufacture having embodied thereon computer-readable program means for improved simulation of a biological system comprising a plurality of chemical reactions, the article of manufacture comprising:

computer-readable program means for *constructing*, using the received user commands and data, *a graphical model of a biological system including a first chemical reaction and a second chemical reaction, the graphical model including a specified constraint provided in addition to the chemical reactions that constrains dynamic behavior of the biological system*;

computer-readable program means for storing the graphical model of the biological system; and

computer-readable program means for *generating, using the constructed graphical model of the biological system, dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint*.

Applicants respectfully urge that Kurata does not disclose at least *computer-readable program means for constructing, using the received user commands and data, a graphical model of a biological system including a first chemical reaction and a second chemical reaction*, which is present in Applicants' claim 16. As discussed above with respect to claim 1, Kurata does not disclose *constructing a graphical model of a biological system including a*

*first chemical reaction and a second chemical reaction.* Kurata also does not disclose *the graphical model including a specified constraint provided in addition to the chemical reactions that constrains dynamic behavior of the biological system and generating, using the constructed graphical model of the biological system, dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction and a second type of computational model for the second chemical reaction and the specified constraint*, which are present in claim 16.

For at least the reasons set forth above, Applicants respectfully urge that Kurata does not anticipate Applicants' claim 16 under 35 U.S.C. §102(b). Therefore, Applicants respectfully request that the above 35 U.S.C. §102(b) rejection of claim 16 be withdrawn.

#### F. Claims 17-22

Claims 17-22 depend from independent claim 16 and, as such, incorporate all of the features of claim 16. For at least the reasons set forth above with respect to claim 16, Applicants respectfully request that the above 35 U.S.C. §102(b) rejection of claims 17-22 be withdrawn.

### V. New Claims

#### A. Claim 45

Applicants' claim 45 recites:

45. A computer-implemented method for simulation of a biological system including a first chemical reaction and a second chemical reaction, the method comprising:

*constructing a graphical model of the biological system including a first chemical reaction and a second chemical reaction;*

*annotating the graphical model in response to a user requesting to add annotations to the model that are provided by the user;*

storing the graphical model of the biological system; and

*generating dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction and a second type of computational model for the second chemical reaction.*

As discussed above, Kurata does not disclose *constructing a graphical model of the biological system including a first chemical reaction and a second chemical reaction*, and *generating dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction and a second type of computational model for the second chemical reaction*, which are present in claim 45.

Furthermore, Applicants respectfully urge that Kurata does not disclose *annotating the graphical model in response to a user requesting to add annotations to the model that are provided by the user*, which is also present in claim 45. Kurata does not contain any disclosure of annotating a model in response to a user request to add annotations to the model.

For at least the reasons set forth above, Applicants respectfully urge that claim 45 is allowable. Therefore, Applicants respectfully request that claim 45 be passed to allowance.

#### **B. Claim 46**

Applicants' claim 46 recites:

46. A computer-readable storage medium holding computer-executable instructions for simulation of a biological system, the medium comprising:

instructions for *constructing a graphical model of the biological system including a first chemical reaction and a second chemical reaction in the biological system*;

instructions for storing the graphical model of the biological system;

instructions for *determining putative reaction times for execution of the first reaction and the second reaction in the graphical model*;

instructions for *sorting the putative reaction times*;

instructions for *executing one of the first reaction and second reaction identified by a first reaction, the first chemical reaction being executed using a first type of computational model and the second chemical reaction being executed using a second type of computational model;*

instructions for recalculating the putative reaction times for the first reaction and the second reaction after executing one of the first reaction and the second reaction identified by the first reaction; and

instructions for resorting the putative reaction times.

As discussed above, Kurata does not disclose at least *constructing a graphical model of the biological system including a first chemical reaction and a second chemical reaction in the biological system, and executing one of the first reaction and second reaction identified by a first reaction, the first chemical reaction being executed using a first type of computational model and the second chemical reaction being executed using a second type of computational model*, which are present in claim 46.

Furthermore, Applicants respectfully submit that Kurata does not disclose at least *determining putative reaction times for execution of the first reaction and the second reaction in the graphical model, and sorting the putative reaction times*, which are also present in claim 46. Kurata does not contain any disclosure of calculating and sorting putative reaction times for execution of the first reaction and the second reaction in the graphical model.

For reasons set forth above, Applicants respectfully urge that claim 46 is allowable. Therefore, Applicants respectfully request that claim 46 be passed to allowance.

### **C. Claim 47**

Claim 47 depends from independent claim 46 and, as such, incorporates all of the features of claim 46. For at least the reasons set forth above with respect to claim 46, Applicants respectfully urge that claim 47 is allowable. Therefore, Applicants respectfully request that claim 46 be passed to allowance.

**VI. Information Disclosure Statement**

Applicants submit herewith an Information Disclosure Statement with references for the Examiner's consideration.

**VII. Conclusion**

In light of the above amendments and arguments, Applicants respectfully submit that all of the pending claims are in condition for allowance. Should the Examiner feel that a teleconference would expedite the prosecution of this application, the Examiner is urged to contact the Applicants' attorney at (617) 227-7400.

Please charge any shortage or credit any overpayment of fees to our Deposit Account No. 12-0080, under Order No. MWS-110. In the event that a petition for an extension of time is required to be submitted herewith, and the requisite petition does not accompany this response, the undersigned hereby petitions under 37 C.F.R. §1.136(a) for an extension of time for as many months as are required to render this submission timely. Any fee due is authorized to be charged to the aforementioned Deposit Account.

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Respectfully submitted,

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